B. NON-TECHNICAL ABSTRACT

The primary immune deficiencies are a group of rare disorders characterized by inherited defects of genes regulating the development and function of the immune system. Although treatment with bone marrow transplant (BMT) can be curative, the majority of patients do not have a matched sibling donor and have a high risk of immunologic complications from mismatched BMT. X-linked severe combined immune deficiency (X-SCID) is the most common form of SCID. X-SCID is caused by mutations in the γc gene, which encodes a cell-surface receptor protein required for the development of lymphocytes. Lymphocytes containing a normal γc gene have a survival advantage over cells with the abnormal γc gene. Gene therapy may be of benefit to patients with X-SCID, by introducing a normal γc gene into immature cells that will differentiate into normal lymphocytes. Our pre-clinical studies have demonstrated that the introduction of the normal γc gene into cells from children with X-SCID can normalize the function of γc receptor function. We propose to test whether introduction of the γc gene into bone marrow or umbilical cord blood cells from infants with X-SCID will lead to the development of normal lymphocytes and clinically beneficial immune function. Gene therapy may offer advantages over mismatched BMT because the use of the patients' own cells will avoid some of the immunological complications of BMT.